Tetrahedron Letters No.53,pp.4619-4622, 1969. Pergamon Press. Printed in Great Britain

A NEW REACTION OF BIS(o-AMINOPHENYL)DISULFIDE WITH KETO-COMPOUNDS. SYNTHESIS OF 1,4-BENZOTHIAZINE SYSTEM.

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(Received in UK 29th September 1969; accepted for publication 14th October 1969)

In recent papers we have reported (1) that bis(o-aminophenyl)disulfide reacts with ketones to afford compounds of type (I) and (II). We have also shown that compounds (I) and (II) arise from the autoxidation of type (III) compounds; the latter can be isolated when the title reaction is run in absence of air.

The structure of bis(o-anil)disulfide was ascribed to compounds (III) mainly on the basis of Raney-Nickel desulfurization which yields the correspondent anil-derivatives, as prevalent products; further evidence came from the observed properties, such as elemental analysis and I.R. spectra. It should be taken into account that remarkable difficulties were encountered in obtaining pure samples of (III) owing to their high sensitivity to oxygen, and to the constant presence in the reaction products, of considerable quantities of benzothiazolines of type(IV).

The results of further experimental work carried out on these compounds (III) bring us to the conclusion that structures of type (III) are incorrect and to assign instead, to the compounds in question, the cyclic structure of 1,4-benzothiazine; furthermore, as proved by the experimental evidence (see table I),some of them are 2H-1,4-benzothiazines, and others 4H-1,4-benzothiazines (see +++).

In fact it was found that the salts of these compounds, obtained in particular conditions, are relatively less sensitive to autoxidation and easier to purify; these salts can be reduced with $NaBH_4$, still in absence of air, to very stable derivatives which can be well characterized. It is possible to assign to the reduction products the structure (VII) on the following evidence: the osmometric determination of molecular weight gives values one half of those calculated for reduced derivatives of type (III). In the I.R. spectra (table I) bands of NH= group are present, while peaks of SH- group are absent. In the N.M.R. spectra

TABLE I

Compd. (°)	M.P. or B.P./mm	I.R. (°°) $\bar{\nu}$, cm^{-1}	Compd. (°)	M.P. or B.P./mm	I.R. (°°) $\bar{\nu}$, cm^{-1} (NH)	N.M.R., δ(°°°) H$_a$	H$_b$	H$_c$
Va	56°	1620 (C=N)	VIIa	62–63°	3380	3,32–3,12 (m)(+)	3,84–3,66 (m)	3,57 (bs)
Vb	64–66°	1620 (C=N)	VIIb	155°/0,1	3400	3,44–3,23 (m)	3,9 –3,68 (m)	3,6 (bs)
Vc	165–7°/0,03	1605 (C=N)	VIIc	84–85°	3420	3,31 (dq)	4,86 (d)	3,98 (bs)
Vd	120–121°	1630(C=N) (*) 1650 (C=C) 3360 (NH)	VIId	195–9°/0,2	3400	4,2 (d)	4–3,76 (m)	3,65 (bs)
Ve	99–100° (2)	1600 (C=N)	VIIe	175–176°	3420	4,39 (d)	4,99 (d)	3,94–3,4 (bs)
VIa	206–208°	1680 (C=C) 3340 (NH)	VIIf	238–240°	3380	3,28–2,92 (m,2H)		3,86 (bs)
VIb	171–173°	1685 (C=C) 3360 (NH)	VIIg	202–203°	3400	3,32–3 (m,2H)		3,39 (bs)

(°) All compounds have satisfactory elemental analyses

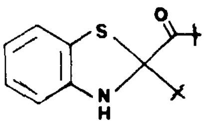
(°°) I.R.spectra of solid compounds were recorded in nujol

(°°°) N.M.R.spectra were recorded with Varian HA-100 spectrometer in $CDCl_3$,using TMS as internal standard

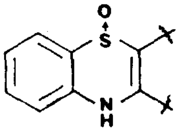
(+) Abbreviation:s=singlet; d=doublet; dq=double quartet; m=multiplet; bs=broad signal

(*) 2-phenyl-3-methyl-1,4-benzothiazine is in the liquid state and in solution a 2H-benzothiazine, while in the solid state is a 4H-benzothiazine

CHART I



(I)



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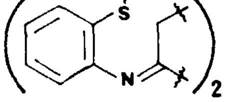

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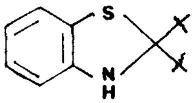

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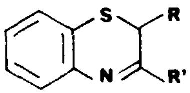

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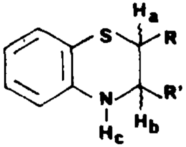
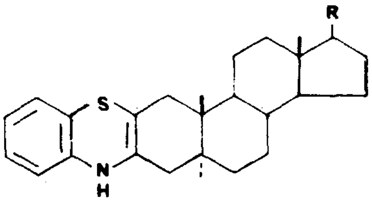
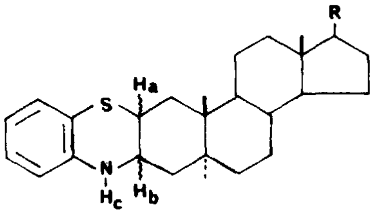


(VII)



(VI)



(VII f,g)

Va, VII a : R=R'= - CH_2-$(CH_2)_3$-CH_2-

Vb, VII b : R=R'= - CH_2-$(CH_2)_4$-CH_2-

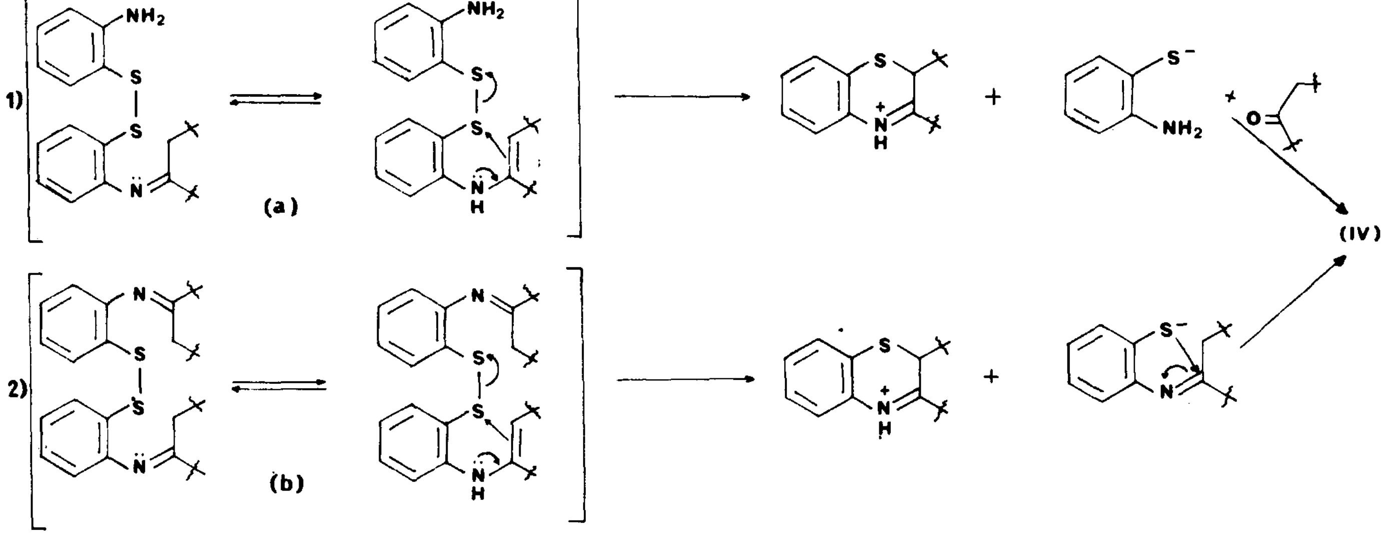
Vc, VII c : R= CH_3; R'=-C_6H_5

Vd, VII d : R= C_6H_5; R'=-CH_3

Ve, VII e : R=R'= -C_6H_5

VIa, VII f : R= -O-CO-CH_3

VIb, VII g : R= $-\underset{\displaystyle CH_3}{CH}-(CH_2)_3-CH-(CH_3)_2$



(table I) signals which can inconfutably be attributed to the two angular protons, characteristic of type (VII) structures, are present. The final proof of structures (V and VI) is given by the identity of our substances with the 1,4-benzothiazines obtained by reacting o-aminothiophenol with the appropriate α-bromoketones.

The reaction of bis(o-aminophenyl)disulfide and ketones appears therefore to be a new method of approach to the 1,4-benzothiazine system. The formation of 1,4-benzothiazines indicates that at a certain stage of the chemical process,the cleavage of -S-S- linkage must occur; this cleavage explains in a more satisfactory way the observed formation of benzothiazolines (IV).

The reaction sequence which could explain the formation of 1,4-benzothiazines (V and VI) together with benzothiazolines (IV) is outlined in chart I.

In view of the general conditions of the reaction between bis(o-aminophenyl) disulfide and ketones (molar ratio 1/2, acid catalysis and water elimination),it seems probable that the first step of the reaction can be either the formation of mono-imines of type (a) or bis-imines of type (b); these first intermediates (a) and (b), in their tautomeric enaminic form, could undergo a cleavage to yield (IV) and (V), owing to the fact that an enaminic β-carbon atom, bearing high electronic density, could attack the -S-S- linkage. When one molar equivalent of ketones is used, only 1,4-benzothiazines and o-aminothiophenol are obtained;this indicates that sequence 1) should be preferred.This particular procedure is an even simpler and practical method for preparing 1,4-benzothiazines. It is also important to note that the 1,4-benzothiazines are those which undergo the autoxidation affording compounds of type (I) and (II), and this particular chemical behaviour has never been reported before.

REFERENCES

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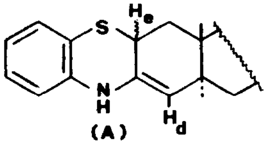
(+++) - The possibility that (VIa,b)could exist in the isomeric structure (A) would seem to be excluded because in the N.M.R. spectra(d_5-pyridine) signals of olefinic (H_d) and angular (H_e) protons are absent.



(A)

Acknowledgement. This work was supported by a research grant from C.N.R. Rome, Italy.